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08/300,510	09/02/1994	MALCOLM L. GEFTER	092.0US	5007

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EXAMINER
SAUNDERS, DAVID A

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 308,510	Applicant(s) GEFTER et al
	Examiner SAUNDERS	Group Art Unit 1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to ~~communication(s) filed on~~ REMAND FROM BPAI.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 108-109, 114-117, 120-123, 128-144 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 108-109, 114-117, 120-123, 128-144 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 10

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

In view of the arguments filed on 6/12/97 (Paper 23), PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

It is noted that the BPAI mailed a remand on 9/19/02. Upon consideration of the remand, the examiner considers it proper to reopen prosecution, with a citation of the Briner et al. reference cited by applicant in Paper 23, at page 3. It is noted that the last page number of this reference is --7612-- not "7613".

The remand has required clarification as to whether or not the amendment of 10/29/98 (Paper 35) has been entered or not. In response, the examiner has directed the entry of this amendment. From what the examiner can tell from the interview summary of 9/22/98 (attached Paper 34), the amendment to claim 108, as filed on 10/29/98, was intended to address concerns raised by the previous examiner regarding Briner et al.

The BPAI also required clarification as to whether the proposed amendment to claim 133 has been entered or not. This amendment was proposed on 12/15/97 (Paper 27) and on 4/8/98 (Paper 30). The examiner has not directed entry of these amendments, since the proposed changes for claim 133 have been incorporated in the amendment of 10/29/98.

Following entry of the amendment of 10/29/98, the claims pending are 108-109, 114-117, 120-123, 128-144. New ground(s) of rejection will be applied to these claims as set forth further below.

To clarify the record the following changes in paper numbering have been entered in the record.

In the lower right hand corner of the "Notification of Non-Compliance" mailed 9/24/98, changed "35" to --34--. The file contents listing does not provide a separate entry for the interview of 9/22/98. This interview will therefore be considered as an attachment to Paper 34.

On form PTO-90 C, mailed 1/22/99, under "Paper Number", changed "33" to --37--.

These changes have been entered in red ink and initialed and dated by the examiner.

Due to entry of the amendment of 10/29/98, the 112, first and second paragraph rejections stated in the examiner's answer of 1/ 22/99 have been withdrawn.

Also, with entry of the amendment of 10/29/98, the 103 rejection stated in the examiner's answer of 11/22/99 is withdrawn.

Sehon et al. teach modifications of allergens which are whole proteins, not peptides.

Litwin et al. teach enyzmatically derived peptide fragments of a protein allergen. The composition is not reproducible. See instant specification page 3, lines 21-27.

Michael et al. likewise teach enzymatically derived fragments of a protein allergen. Like issues regarding reproducibility would apply to this reference.

Kuo (5,328,991) is the most relevant reference. It is noted that Kuo vaguely refers to "portions thereof" with respect to the TRFP (Fel d I) protein as having therapeutic activity (col. 7, lines 42-47). Kuo gives no direction that these "portions" should represent "at least about 20% of the T-cell epitopes recognized by T-cell receptors" specific for the protein allergen.

New grounds of rejection under 112 first and second paragraphs are stated as follows.

Claims 108-109, 114-117, 120-123 and 128-144 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 108 lines 5-6 "about 20% of the T cell epitopes recognized by T-cell receptors" is unclear, because it is not clear whether this refers to 20% of the T-cell receptors in the particular human being treated or to 20% of the T-cell receptors of an aggregate of several individuals within the human, population (it is not even clear if the "T-cell" receptors are human). It is believed applicant intends the latter; however, applicant should respond by pointing out what portion of the specification teaches what is intended and by entering appropriate clarifying language therefrom.

In claims 136-137 "said initial treatment" lacks antecedent basis.

Claims 108-109, 114-117, 120-123 and 128-144 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain new matter.

Claim 108 recites new matter by reciting "not being conjugated to another molecule". The examiner notes that this concept is taught at page 5, line 24; however this is recited in the context of defining an "isolated" peptide, and the examiner sees nothing in claim 108 that requires the peptide to be "isolated".

Claims 115 and 117 contain new matter by reciting "about" before each percentage value. There is no recitation of "about" at specification page 14, line 5.

Claim 134 recites new matter because its recitation does not follow the language of original claim 36 nor of specification page 18, lines 37-38. The new language is broader. The original language required injections at intervals of "once a week"; the new language does not stipulate any intervals at all. The original language required that the series of injections conclude at "3-6 weeks"; the new language merely requires that these conclude at 6 weeks. Dependent claim 115 is included in the rejection.

In claims 139-144, it is not clear where each recited percentage of "improvement" is supported by the original disclosure. If these values are derived from Fig. 1, applicant is requested to show the calculations from the data presented in Fig. 1 that arrived at the recited values. In any event, even if applicant can show how these percentages were calculated, it is

considered that each would be overly broad, because each would have been disclosed as having been achieved in the context of a particular peptide dosage, given for a specific number of times at specific intervals, none of which are recited.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

> (f) he did not himself invent the subject matter sought to be patented.

Claims 108-109, 114-117, 120-123 and 128-133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Briner et al. (PNAS, 90, 7608-7612, 1993).

Briner et al's. disclosure has exemplified all aspects of claim 108 except for the fact that mice, instead of humans, are treated with peptides from the Fel d I protein allergen. As to the treatment of humans, it is clear that Briner et al. envision like treatments of humans. See especially page 7608, col. 2, first full paragraph; pages 7611-712, paragraph spanning; and page 7612, cols. 1 and 2, paragraph spanning. It is to be noted that (1) Briner et al. disclose (pg. 7611, col. 1) the two peptides of Fel d I which "account for the majority of human T-cell reactivity" ("majority" is taken to be greater than 50%; which is greater than "about 20%" recited in claim 108); (2) Briner et al. teach that s.c. administration of the two peptides IPC-1 and IPC-2 can tolerize mice against the Fel d I protein (page 7611, cols. 1-2, para. spanning); (3) Briner et al. teach that a tolerizing treatment with even one of these two peptides, IPC-1, can tolerize T-cells in animals having a preexisting response to the protein allergen (page 7610 cols. 1-2, para spanning); (4) Briner et al. teach how to synthesize and formulate the peptides for S.C. injection; (5) Briner et al. teach that treatment with the two exemplified peptides can tolerize and that it is not necessary to tolerize all T-cells against all epitopes of a protein allergen (page 7611, col. 2, first full para.).

Because of all of these factors one would have had a reasonable expectation of success in using the IPC-1 and/or IPC-2 peptides of Briner et al. in treating humans.

A reasonable expectation of success is all that is required. In re O'Farrell 7 USPQ2d 1673. The fact that a lot of routine testing might be required to confirm results in humans (e.g. to meet FDA regulations) does not detract from the fact that Briner et al. reasonably enable the

treatment of humans without undue experimentation, given their results in mice. See In re Wands 8 USPQ2d 1400 regarding routine testing.

Regarding dependent claim 14, this is rejected because a typical T-cell epitope is less than the 27 residue length of the IPC-1 and IPC-2 peptides of Briner et al. Therefore it can be properly considered that each these peptides has "at least one amino acid... addition" to the T-cell eptiope. For the length of a typical T-cell epitope see Janeway et al. --teaching 8-10 residues for class I and 13-17 residues for class II.

The IPC-1 and IPC-2 peptide are consistent with the limitations of instant claims 109 and 120-121.

Regarding claims 122-123, cats are considered to be of the genus Felis, and Fel d I is recited in claim 123.

The PBS used as a diluent by Briner et al. is consistent with the carrier of claims 128-129 and the solution of claim 130.

The S.C. tolerizing treatment of Briner et al. is consistent with claims 131-132.

The treatments of Briner et al. are "without adjuvant" as recited in claim 133 (page 7612, col. 1, first full para.).

With respect to the percent purity limitations of instant claims 115-117, it is noted that Briner et al. do not teach any specific percentage of purity. However, their peptides were prepared with the use of the Merrifield solid phase synthesis method. The peptides were then purified via HPLC, and analyzed for amino acid content. These steps correspond to those

disclosed by applicant at specification page 14. It is thus considered that what Briner et al. did would inherently provide peptides of the recited degree of purity. Alternatively it would have been obvious to set the recited limits in order to meet regulatory requirements (e.g. FDA) so that the peptides could be administered to humans. Further, applicant has admitted (page 14, lines 4-8) that is was art known how to purify synthetic peptides to the stated degrees of purity.

With respect to claim 138, recitation of "statistically significant" would have been obvious since such is routinely required by regulators (e.g. FDA) prior to approval of any pharmaceutical for human use.

Claims 108, 114-115, 120-123, 129, 131 and 133 are rejected under 35 U.S.C. 102(b) or (e) as being anticipated by Rogers et al. (WO 93/08280 or U.S. 5,547,669), as evidenced by Briner et al.

The two Rogers et al. patent publications are equivalent. For convenience, the examiner will refer by col. and line number to the U.S. patent.

Rogers et al. teach recombinately produced "recombinotope peptides" --e.g. containing the sequences of three T-cell epitopes of Fel d I. As such these recombinotope peptides are "reproducible". These are taught as being produced with a purity of greater than 90% (col. 21, lines 62-65).

From the criteria for selecting the T-cell epitopes for incorporation within the exemplified recombinotopes (see Ex. 1 at cols 17-18), it is considered that those selected would inherently account for "at least about 20% of the T-cell epitopes recognized by T-cell receptors". Also, it is

noted that segments X and Y of Rogers et al. (col. 18, lines 12+) correspond to peptides that "account for the majority of human T-cell reactivity to Fel d I" (Briner et al. at page 7611, col. 1); this statement thus provides extrinsic evidence that the eptiopes selected by Rogers et al. account for "at least about 20% of the T-cell eptiopes recognized by T-cell receptors".

Rogers et al. teach therapy at col. 3, lines 47-55; col. 9, lines 31-45; col. 12, line 31 - col. 13, line 2; and col. 14, lines 25-64 for example.

From the above considerations it is clear that Rogers et al. anticipate instant claims 108, 115, 120, 122-123, and 128.

Regarding dependent claims 114, this is considered anticipated, since any of the peptides comprising epitopes X, Y and Z, as exemplified by Rogers et al.,.may be considered as one of these epitopes with "at least one amino acid addition" (the "addition" being the other two epitopes).

Regarding claim 121, note col. 12, line 64 - col. 13, line 2.

With respect to claims 129 and 131 note col. 12, lines 42-51.

Regarding claim 133, Rogers et al. teach administration of adjuvant as optional (col. 12, lines 40-43). Thus the administration of the peptides without adjuvant is encompassed.

Claims 108 and 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rogers et al.

Claim 138 is rejected as obvious, following the rational stated supra for Briner et al.

Claims 108-109, 114, 120-123 and 128-133 are rejected under 35 U.S.C. 102(a) as being anticipated by Gefter et al. (WO 93/19178) in light of Briner et al.

Gefter et al. show essentially the same experiments as Briner et al., noted further supra, employing subcutaneous injection of peptide X and Y (corresponding to peptides IPC-1 and IPC-2 of Briner et al.), which (as argued supra in the rejections over Briner et al. and Rogers et al.) constitute "at least about 20% of the T-cell epitopes recognized by T-cell receptors". For use of these peptides in human therapy and the pharmaceutically acceptable carriers employed therewith, note pages 20-30. From these considerations claims 108-109, 120-123 and 128-132 are clearly anticipated.

Regarding claim 114, note teachings of various modifications to the peptides at pages 28-29.

With respect to claim 133 the experiments in the examples employ subcutaneous injection without adjuvant.

Claims 108, 115-117 and 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gefter et al. (WO 93/19178)

As argued supra with respect to Briner et al. it is considered that one would have been motivated to obtain peptides with the recited degree of purity and that such degrees of purity were inherently obtained or, at the least, would have been routinely obtainable by art known methods of purifying synthetic peptides. Claim 138 is rejected following the rational stated for Briner et al.

Claims 108 and 136 are rejected under 35 U.S.C. 103(a) as being unpatentable over Briner et al. in view of Litwin et al.

Claims 108 and 136 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rogers et al. in view of Litwin et al.

Claims 108 and 136 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gefter et al. in view of Litwin et al.

Each primary reference has been cited supra for teaching the use of T-cell epitopic peptides of Fel d I for treating allergy. Litwin et al. show that, in treating allergic patients with a mixture of peptides containing T-cell epitopes, it was known to increase the subcutaneously administered doses gradually, during an initial treatment regimen (page 459, col. 2). It appears that this manner of treatment was for the purpose of minimizing the occurrences of undesirable local or systemic reactions. It would have been obvious to likewise administer the peptides of Briber et al., Rogers et al., or Gefter et al. according to a regimen that would permit one to check for adverse reactions to the treatment, before giving the highest doses.

Claims 108-109, 115-116. 120-123, and 128-133 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. The above claims have been rejected under 102(a), (b), or (e) over one or both of Rogers et al. and Gefter et al.

What is it about the instant, later filed application that uniquely distinguishes the claimed invention from disclosures earlier filed by the same assignee? The assignee appears to be "overly active" in filing multiple redundant disclosures with claims to common subject matter.

Attached hereto is a signed form PTO-1449, from an IDS filled on 8/23/95 (Paper 10).

An IDS was also filed on 12/12/95 (Paper 17). The examiner can find no form PTO-1449 for this, and it is not clear if there are any references cited therein that are still in the file wrapper. Applicant is requested to clarify whether a copy of the signed form PTO-1449 is in his file and to provide a copy of this.

On attached form PTO-892, a copy of Briner et al. has not been supplied to applicant because applicant supplied a copy with an earlier response.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

November 13, 2002

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644